REMARKS

In the Office Action dated January 15, 2003, claims 33, 35-36, 41-42, 45, 48-49, 57-59, 62, 64, 75-83, 88-93, 97-99 and 101-210, were rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Claims 33, 35-36, 41-42, 45, 48-49, 57-59, 62, 64, 75-83, 88-93, 97-99 and 101-210 were also rejected for alleged obviousness-type double-patenting in view of claims 18-42 of U.S. Patent No. 6,503,894, and were provisionally rejected for alleged obviousness-type double-patenting in view of claims 1-21, 27, 53-55, 57-58, 60-64, and 79-145 of co-pending U.S. Application No. 10/033,101. Claims 33, 35-36, 41-42, 45, 48-49, 57-59, 62, 64, 75-83, 88-93, 97-99 and 101-210 have been cancelled. Upon entry of this Amendment, new claims 211-394 are pending and under consideration in the present application. The Examiner's withdrawal of the 35 U.S.C. § 103(a) rejection of claims 33, 35, 36, 41, 42, 45, 48, 49, 57-59, 62, 64, 75-83, 88-93, 97-99 and 101-210 is acknowledged.

Applicant respectfully submits that no new matter has been added by way of this amendment.

IN THE CLAIMS

Please delete claims 33, 35-36, 41-42, 45, 48-49, 57-59, 62, 64, 75-83, 88-93, 97-99 and 101-210.

Please add new claims 211-394 as follows:

211. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject, wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction.

212. (New) The method of claim 211, wherein the pharmaceutical comprises at least one of: sildenafil citrate, pentoxifylline, yohimbine, apomorphine, alprostadil, papaverine, or phentolamine, or a combination, salt, or enantiomer thereof.

213. (New) The method of claim 211, wherein the pharmaceutical comprises at least one of a phosphodiesterase inhibitor or a dopamine receptor agonist, or a combination, salt, or enantiomer thereof.

214. (New) The method of claim 213, wherein the phosphodiesterase inhibitor is at least one of type III, type IV, or type V and mixtures thereof.

215. (New) The method of claim 214, wherein the phosphodiesterase inhibitor is type V.

216. (New) The method of claim 211, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

217. (New) The method of claim 211, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

218. (New) The method of claim 211, wherein the composition comprises testosterone, alcohol, a penetration enhancer, and a gelling agent.

219. (New) The method of claim 218, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

220. (New) The method of claim 219, wherein the penetration enhancer is isopropyl myristate.

221. (New) The method of claim 218, wherein the gelling agent comprises polyacrylic acid.

222. (New) The method of claim 218, wherein the alcohol is selected from the group consisting of: ethanol and isopropyl.

223. (New) The method of claim 218, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

224. (New) The method of claim 223, wherein the composition further comprises sodium hydroxide.

225. (New) The method of claim 224, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

226. (New) The method of claim 211, wherein the composition and the pharmaceutical are components of a kit.

227. (New) The method of claim 211, wherein the subject is eugonadal or hypogonadal.

228. (New) The method of claim 211, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

229. (New) The method of claim 211, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

230. (New) The method of claim 211, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

231. (New) The method of claim 211, wherein the composition is administered at least once per day.

232. (New) The method of claim 231, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

233. (New) The method of claim 233, wherein the composition is administered to the subject for approximately 7 days.

234. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject, wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction, and

wherein the method is more effective in treating erectile dysfunction than a method comprising the administration of either the pharmaceutical or the composition alone.

235. (New) The method of claim 234, wherein the pharmaceutical comprises at least one of: sildenafil citrate, pentoxifylline, yohimbine, apomorphine, alprostadil, papaverine, or phentolamine, or a combination, salt, or enantiomer thereof.

236. (New) The method of claim 234, wherein the pharmaceutical comprises at least one of a phosphodiesterase inhibitor or a dopamine receptor agonist, or a combination, salt, or enantiomer thereof.

237. (New) The method of claim 236, wherein the phosphodiesterase inhibitor is at least one of type III, type IV, or type V, and mixtures thereof.

238. (New) The method of claim 237, wherein the phosphodiesterase inhibitor is type V.

239. (New) The method of claim 234, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

240. (New) The method of claim 234, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

241. (New) The method of claim 234, wherein the composition comprises testosterone, alcohol, a penetration enhancer, and a gelling agent.

242. (New) The method of claim 241, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

243. (New) The method of claim 242, wherein the penetration enhancer is isopropyl myristate.

244. (New) The method of claim 241, wherein the gelling agent comprises polyacrylic acid.

245. (New) The method of claim 241, wherein the alcohol is selected from the group consisting of: ethanol and isopropyl.

246. (New) The method of claim 241, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

247. (New) The method of claim 246, wherein the composition further comprises sodium hydroxide.

248. (New) The method of claim 247, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

249. (New) The method of claim 234, wherein the composition and the pharmaceutical are components of a kit.

250. (New) The method of claim 234, wherein the subject is eugonadal or hypogonadal.

251. (New) The method of claim 234, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

252. (New) The method of claim 234, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

253. (New) The method of claim 234, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

254. (New) The method of claim 234, wherein the composition is administered at least once per day.

255. (New) The method of claim 254, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

256. (New) The method of claim 255, wherein the composition is administered to the subject for approximately 7 days.

257. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject, wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction, and

wherein the method results in a synergistic effect.

258. (New) The method of claim 257, wherein the pharmaceutical comprises at least one of: sildenafil citrate, pentoxifylline, yohimbine, apomorphine, alprostadil, papaverine, or phentolamine, or a combination, salt, or enantiomer thereof.

259. (New) The method of claim 257, wherein the pharmaceutical comprises at least one of a phosphodiesterase inhibitor or a dopamine receptor agonist, or a combination, salt, or enantiomer thereof.

260. (New) The method of claim 259, wherein the phosphodiesterase inhibitor is at least one of type III, type IV, or type V, and mixtures thereof.

261. (New) The method of claim 260, wherein the phosphodiesterase inhibitor is type V.

262. (New) The method of claim 257, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

263. (New) The method of claim 257, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

264. (New) The method of claim 257, wherein the composition comprises testosterone, alcohol, a penetration enhancer, and a gelling agent.

265. (New) The method of claim 264, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

266. (New) The method of claim 265, wherein the penetration enhancer is isopropyl myristate.

267. (New) The method of claim 264, wherein the gelling agent comprises polyacrylic acid.

268. (New) The method of claim 264, wherein the alcohol is selected from the group consisting of: ethanol and isopropyl.

269. (New) The method of claim 264, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

270. (New) The method of claim 269, wherein the composition further comprises sodium hydroxide.

271. (New) The method of claim 270, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

272. (New) The method of claim 257, wherein the composition and the pharmaceutical are components of a kit.

273. (New) The method of claim 257, wherein the subject is eugonadal or hypogonadal.

274. (New) The method of claim 257, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

275. (New) The method of claim 257, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

276. (New) The method of claim 257, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

277. (New) The method of claim 257, wherein the composition is administered at least once per day.

278. (New) The method of claim 277, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

279. (New) The method of claim 278, wherein the composition is administered to the subject for approximately 7 days.

280. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject, wherein the pharmaceutical is selected from the group consisting of: phosphodiesterase inhibitors and dopamine receptor agonists,

wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction.

281. (New) The method of claim 280, wherein the pharmaceutical comprises sildenafil citrate or apomorphine or a combination, salt, or enantiomer thereof.

282. (New) The method of claim 280, wherein the phosphodiesterase inhibitor is at least one of type III, type IV, or type V, and mixtures thereof.

283. (New) The method of claim 282, wherein the phosphodiesterase inhibitor is type V.

284. (New) The method of claim 280, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

285. (New) The method of claim 280, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

286. (New) The method of claim 280, wherein the composition comprises testosterone, alcohol, a penetration enhancer, and a gelling agent.

287. (New) The method of claim 286, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

288. (New) The method of claim 287, wherein the penetration enhancer is isopropyl myristate.

289. (New) The method of claim 286, wherein the gelling agent comprises polyacrylic acid.

290. (New) The method of claim 286, wherein the alcohol is selected from the group consisting of: ethanol and isopropyl.

291. (New) The method of claim 286, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

292. (New) The method of claim 291, wherein the composition further comprises sodium hydroxide.

293. (New) The method of claim 292, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

294. (New) The method of claim 280, wherein the composition and the pharmaceutical are components of a kit.

295. (New) The method of claim 280, wherein the subject is eugonadal or hypogonadal.

296. (New) The method of claim 280, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

297. (New) The method of claim 280, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

298. (New) The method of claim 280, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

299. (New) The method of claim 280, wherein the composition is administered at least once per day.

300. (New) The method of claim 299, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

301. (New) The method of claim 300, wherein the composition is administered to the subject for approximately 7 days.

302. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject selected from the group consisting of: sildenafil citrate, pentoxifylline, yohimbine, apomorphine, alprostadil, papaverine, and phentolamine,

wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction.

303. (New) The method of claim 302, wherein the pharmaceutical comprises sildenafil citrate or apomorphine or a combination, salt, or enantiomer thereof.

304. (New) The method of claim 302, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

305. (New) The method of claim 302, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

306. (New) The method of claim 302, wherein the composition comprises testosterone, alcohol, a penetration enhancer, and a gelling agent.

307. (New) The method of claim 306, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

308. (New) The method of claim 307, wherein the penetration enhancer is isopropyl myristate.

309. (New) The method of claim 306, wherein the gelling agent comprises polyacrylic acid.

310. (New) The method of claim 306, wherein the alcohol is selected from the group consisting of: ethanol and isopropyl.

311. (New) The method of claim 306, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

312. (New) The method of claim 311, wherein the composition further comprises sodium hydroxide.

313. (New) The method of claim 312, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

314. (New) The method of claim 302, wherein the composition and the pharmaceutical are components of a kit.

315. (New) The method of claim 302, wherein the subject is eugonadal or hypogonadal.

316. (New) The method of claim 302, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

317. (New) The method of claim 302, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

318. (New) The method of claim 302, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

319. (New) The method of claim 302, wherein the composition is administered at least once per day.

320. (New) The method of claim 319, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

321. (New) The method of claim 320, wherein the composition is administered to the subject for approximately 7 days.

322. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone, a gelling agent, and a penetration enhancer to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject selected from the group consisting of: sildenafil citrate, pentoxifylline, yohimbine, apomorphine, alprostadil, papaverine, and phentolamine,

wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction.

323. (New) The method of claim 322, wherein the pharmaceutical comprises sildenafil citrate or apomorphine or a combination, salt, or enantiomer thereof.

324. (New) The method of claim 322, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

325. (New) The method of claim 322, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

326. (New) The method of claim 322, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

327. (New) The method of claim 326, wherein the penetration enhancer is isopropyl myristate.

328. (New) The method of claim 322, wherein the gelling agent comprises polyacrylic acid.

329. (New) The method of claim 322, wherein the composition comprises alcohol selected from the group consisting of: ethanol and isopropyl.

330. (New) The method of claim 322, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

331. (New) The method of claim 330, wherein the composition further comprises sodium hydroxide.

332. (New) The method of claim 331, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

333. (New) The method of claim 322, wherein the composition and the pharmaceutical are components of a kit.

334. (New) The method of claim 322, wherein the subject is eugonadal or hypogonadal.

335. (New) The method of claim 322, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

336. (New) The method of claim 322, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

337. (New) The method of claim 322, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

338. (New) The method of claim 322, wherein the composition is administered at least once per day.

339. (New) The method of claim 338, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

340. (New) The method of claim 339, wherein the composition is administered to the subject for approximately 7 days.

341. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone, a gelling agent, and a penetration enhancer to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject,

wherein the pharmaceutical is sildenafil citrate or apomorphine, or a combination, salt, or enantiomer thereof; and

wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction.

342. (New) The method of claim 341, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

343. (New) The method of claim 341, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

344. (New) The method of claim 341, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate,

glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

345. (New) The method of claim 344, wherein the penetration enhancer is isopropyl myristate.

346. (New) The method of claim 341, wherein the gelling agent comprises polyacrylic acid.

347. (New) The method of claim 341, wherein the composition further comprises alcohol selected from the group consisting of: ethanol and isopropyl.

348. (New) The method of claim 341, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

349. (New) The method of claim 348, wherein the composition further comprises sodium hydroxide.

350. (New) The method of claim 349, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide

dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

351. (New) The method of claim 341, wherein the composition and the pharmaceutical are components of a kit.

352. (New) The method of claim 341, wherein the subject is eugonadal or hypogonadal.

353. (New) The method of claim 341, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

354. (New) The method of claim 341, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

355. (New) The method of claim 341, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

356. (New) The method of claim 341, wherein the composition is administered at least once per day.

357. (New) The method of claim 356, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

358. (New) The method of claim 357, wherein the composition is administered to the subject for approximately 7 days.

359. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone, a gelling agent, and a penetration enhancer to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject, wherein the pharmaceutical is sildenafil citrate or apomorphine, or a combination, salt, or enantiomer thereof;

wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction, and

wherein the method is more effective in treating erectile dysfunction than a method comprising the administration of either the pharmaceutical or the composition alone.

360. (New) The method of claim 359, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

361. (New) The method of claim 359, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

362. (New) The method of claim 359, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

363. (New) The method of claim 362, wherein the penetration enhancer is isopropyl myristate.

364. (New) The method of claim 359, wherein the gelling agent comprises polyacrylic acid.

365. (New) The method of claim 359, wherein the composition further comprises alcohol selected from the group consisting of: ethanol and isopropyl.

366. (New) The method of claim 359, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

367. (New) The method of claim 366, wherein the composition further comprises sodium hydroxide.

368. (New) The method of claim 367, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

369. (New) The method of claim 359, wherein the composition and the pharmaceutical are components of a kit.

370. (New) The method of claim 359, wherein the subject is eugonadal or hypogonadal.

371. (New) The method of claim 359, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

372. (New) The method of claim 359, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

373. (New) The method of claim 359, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

374. (New) The method of claim 359, wherein the composition is administered at least once per day.

375. (New) The method of claim 374, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

376. (New) The method of claim 375, wherein the composition is administered to the subject for approximately 7 days.

377. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone, a gelling agent, and a penetration enhancer to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject,

wherein the pharmaceutical is sildenafil citrate or apomorphine, or a combination, salt, or enantiomer thereof;

wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction, and

wherein the method results in a synergistic effect.

378. (New) The method of claim 377, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

379. (New) The method of claim 377, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

380. (New) The method of claim 377, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

381. (New) The method of claim 380, wherein the penetration enhancer is isopropyl myristate.

382. (New) The method of claim 377, wherein the gelling agent comprises polyacrylic acid.

383. (New) The method of claim 377, wherein the composition further comprises alcohol selected from the group consisting of: ethanol and isopropyl.

384. (New) The method of claim 377, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

385. (New) The method of claim 384, wherein the composition further comprises sodium hydroxide.

386. (New) The method of claim 385, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

387. (New) The method of claim 377, wherein the composition and the pharmaceutical are components of a kit.

388. (New) The method of claim 377, wherein the subject is eugonadal or hypogonadal.

389. (New) The method of claim 377, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

390. (New) The method of claim 377, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

391. (New) The method of claim 377, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

392. (New) The method of claim 377, wherein the composition is administered at least once per day.

393. (New) The method of claim 392, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

394. (New) The method of claim 393, wherein the composition is administered to the subject for approximately 7 days.

I. Amendments to the Claims

Claims 33, 35-36, 41-42, 45, 48-49, 57-59, 62, 64, 75-83, 88-93, 97-99 and 101-210 have been cancelled. New claims 211-394 have been added and are currently pending. Instead of amending the old claims, Applicant has rewritten the claims in order to facilitate ease of reading and to advance prosecution. As such, no new matter has been added by the way of these amendments. Applicant is not aware of any prior art that would affect the patentability of new claims 211-394.

II. Rejections under 35 U.S.C. § 112, first paragraph

Claims 33, 35-36, 41-42, 45, 48-49, 57-59, 62, 64, 75-83, 88-93, 97-99 and 101-210 were rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Claims 33, 35-36, 41-42, 45, 48-49, 57-59, 62, 64, 75-83, 88-93, 97-99 and 101-210 have been cancelled. New claims 211-394 are pending. Applicant will address the rejection in light of pending claims 211-394. Specifically, the Office argues that while Applicant's specification is enabling for testosterone in the methods of the invention, the specification is not enabling for claims to improving the efficacy of any pharmaceutical useful for treating erectile dysfunction in a male subject. This rejection is respectfully traversed.

Applicant claims methods for treating erectile dysfunction in a male subject comprising administering in combination a topical gel or cream composition comprising testosterone to a male subject and a pharmaceutical useful for treating erectile dysfunction in a male subject, wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction. Exemplary pharmaceuticals useful for treating erectile dysfunction are known in the art, and are described in the specification, at, for

example, page 2, line 10, through page 3, line 5 (VIAGRA® (sildenafil citrate USP), pentoxifylline (TRENTAL®), yohimbine hydrochloride (ACTIBINE®, YOCON®, YOHIMEX®), apomorphine (UPRIMA®), alprostadil (the MUSE® system, TOPIGLAN®, CAVERJECT®), papaverine (PAVABID®, CERESPAN®), and phentolamine (VASOMAX®, REGITINE®); Example 6; and the claims. Specific classes of pharmaceuticals useful treating erectile dysfunction are known in the art, and include, e.g., phosphodiesterase inhibitors and dopamine receptor agonists. Specification at, for example, page 2, line 10, through page 3, line 5; Example 6; and the claims.

The Office argues that the specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Specifically, the Office states on page 4 of the Office Action of January 15, 2003:

> In the instant case, "a pharmaceutical" may encompass any pharmaceuticals. However, Applicant's specification provides the experimental results showing that only testosterone was [sic] improved the efficacy by employing the instant composition for treating erectile dysfunction in a male subject. Thus, these examples fail to provide sufficient working examples to support the broad use of any "pharmaceutical" in the claimed method for improving the efficacy. ... Hence, the instant claims read on the employment of any "pharmaceutical" in pharmaceutical methods useful in male subject treatments, necessitating one of skill to perform an exhaustive search for the embodiments of "pharmaceutical" suitable to practice the claimed invention.

The Office appears to be arguing that Applicant's claims are not enabled because the scope of the language "a pharmaceutical" in the claims would necessitate one of skill in the art to exhaustively search for pharmaceuticals suitable to practice the claimed invention. Applicant respectfully disagrees.

Applicant's claims specifically require that the pharmaceutical be "useful for treating erectile dysfunction in a male subject." As such, the language "a pharmaceutical" in Applicant's claims is not viewed in isolation as encompassing any pharmaceuticals, as alleged by the Office, but is viewed in the context of the claims, which state "a pharmaceutical useful for treating erectile dysfunction in a male subject." As stated above and in the specification, pharmaceuticals useful for treating erectile dysfunction in a male subject are widely known in the art and easily available. For example, VIAGRA®, a widely used pharmaceutical useful for treating erectile dysfunction in a male subject, had $1.5 billion in sales in 2001. (Pfizer 2001 Annual Report). Thus, one ordinarily skilled in the art would not have to exhaustively search for a pharmaceutical suitable to practice the claimed

invention, but can merely pick any pharmaceutical from a small, defined subset of pharmaceuticals, namely those useful for treating erectile dysfunction in a male subject.

It is well settled that the burden of establishing a *prima facie* case of lack of enablement rests on the Office. *In re Marzocchi,* 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971) ("In any event, it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.") In order to establish a *prima facie* case of lack of enablement, the Office must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure. *In re Wright,* 999 F. 2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993).

Applicant respectfully submits that the Office has not met this burden. Applicant has claimed methods of treating erectile dysfunction in a male subject by administering in combination a testosterone gel or cream along with a pharmaceutical of a defined class of pharmaceuticals (i.e. pharmaceuticals useful for treating erectile dysfunction in a male subject) and has set forth examples of suitable pharmaceuticals within the class. Suitable pharmaceuticals are commercially available and easily discernable by one ordinarily skilled in the art. Applicant's inventions are enabled for the use of the testosterone composition. (See, e.g., Office Action of January 15, 2003, at page 4). As such, one of skill in the art could easily practice Applicant's claimed methods without undue experimentation. The Office has failed to set forth a specific argument or factual evidence as to why one of ordinary skill in the art would not be able to practice Applicant's invention without undue experimentation and has not provided reasons to doubt the objective truth of Applicant's specification. The Office may not improperly shift the burden of proving that the specification provides an enabling disclosure onto the Applicant in this manner.

To illustrate, in *Ex Parte Charles T. Esmon and Philip C. Comp,* the Board of Patent Appeals and Interferences held that a claimed subject matter directed to "a compound eliciting production of cytokine in the patient" was properly enabled by guidance in the specification as to the types of cytokines, including functional definitions and examples of specific compounds, which are useful in the claimed invention, where the examiner did not properly explain "why one skilled in the art would have undue difficulty in identifying

compounds which elicit production of such cytokines." Appeal No. 1997-3951, page 7. (unpublished). The Examiner in the case argued:

> The claims encompass any compound which elicits production of any cytokine. The scope of the claims is not commensurate with the evidence of enablement provided by the disclosure with regard to the extremely large number of compounds and cytokines broadly encompassed by the claims...

Id., at page 4. The specification at issue disclosed specific functional classes of compounds suitable for eliciting production of cytokine in the patient and listed specific examples of suitable compounds. *Id.*, at pages 6-7. Thus, the Board held that the claims were properly enabled and reversed the rejections under 35 U.S.C. § 112, first paragraph.

In view of the above, the rejection of the claims under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement is improper and should be withdrawn.

II. Rejections under the Judicially-Created Doctrine of Obviousness-Type Double Patenting

The Office rejected claims 33, 35-36, 41-42, 45, 48-49, 57-59, 62, 64, 75-83, 88-93, 97-99 and 101-210 for obviousness-type double patenting in view of claims 18-42 of U.S. Patent No. 6,503,894. The Office also provisionally rejected claims 33, 35-36, 41-42, 45, 48-49, 57-59, 62, 64, 75-83, 88-93, 97-99 and 101-210 for obviousness-type double patenting in view of claims 1-21, 27, 53-55, 57-58, 60-64, and 79-145 of co-pending U.S. Application No. 10/033,101. Claims 33, 35-36, 41-42, 45, 48-49, 57-59, 62, 64, 75-83, 88-93, 97-99 and 101-210 have been cancelled. New claims 211-394 are pending. Applicant will address the rejection in light of pending claims 211-394. These rejections are respectfully traversed.

Claims 18-42 of U.S. Patent No. 6,503,894 (the '894 patent) are generally drawn to methods for administering an active agent to a human subject in need thereof, comprising providing a testosterone pharmaceutical composition and applying a daily dose of the composition to the skin of the subject. Claims 18-42 of the '894 patent do not claim or suggest methods for improving the efficacy of a pharmaceutical useful for treating erectile dysfunction in a male subject, comprising administering to an area of skin of the subject a pharmacologically effective amount of a testosterone composition.

Claims 1-21, 27, 53-55, 57-58, 60-64, and 79-145 of co-pending U.S. Application No. 10/033,101 (the '101 application) are generally directed to methods of transdermally delivering testosterone to a male subject to treat hypogonadism by applying a hydroalcoholic gel to skin of the male subject. Claims 1-21, 27, 53-55, 57-58, 60-64, and 79-145 of the '101

application do not claim or suggest methods for improving the efficacy of a pharmaceutical useful for treating erectile dysfunction in a male subject, comprising administering to an area of skin of the subject a pharmacologically effective amount of a testosterone composition.

Applicant, on the other hand, claims methods for treating erectile dysfunction in a male subject comprising administering in combination a topical gel or cream composition comprising testosterone to a male subject and a pharmaceutical useful for treating erectile dysfunction in a male subject, wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction. Because neither the claims of the '894 patent, nor the claims of the '101 application teach or suggest the subject matter of Applicant's claims, the obviousness-type double patenting rejections are improper and withdrawal of these rejections is respectfully requested.

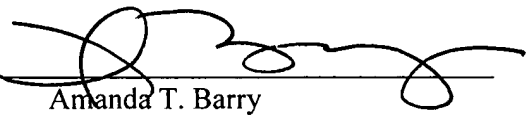
To establish obviousness-type double patenting, the Office must show that the claimed inventions are not patentably distinct and are based on a *prima facie* showing of obviousness. *In re Vogel*, 422 F.2d 438, 441, 164 U.S.P.Q. 619, 621-622 (C.C.P.A. 1970). The Office must present clear evidence to establish why the variation would be obvious. *In re Kaplan,* 789 F.2d 1574, 1578, 229 U.S.P.Q. 678, 682 (Fed. Cir. 1986); *Ex parte Davis*, 56 U.S.P.Q.2d 1434, 1437-1438 (Bd. Pat. App. Int. 2000) (unpublished). The Office may not use the disclosure of the patent or patent application upon which the rejection is based as prior art. *In re Aldrich,* 398 F.2d 855, 859, 158 U.S.P.Q. 311, 313-314 (CCPA 1968). Furthermore, the Office must compare the properly interpreted claims as a whole. *General Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1278, 23 U.S.P.Q.2d 1839, 1843 (Fed. Cir. 1992).

Applicant respectfully submits that the Office has not shown that the claimed inventions are not patentably distinct and has not presented a *prima facie* case of obviousness-type double patenting. The Office has not presented any evidence to establish why the variation would be obvious, and has merely made broad, sweeping statements as to obviousness. As such, the Office has not shown that either the claims of the '894 patent or the claims of the '101 application teach or suggest the subject matter of Applicant's claims, and withdrawal of the rejections of the claims for obviousness-type double patenting in view of claims 18-42 of U.S. Patent No. 6,503,894 and in view of claims 1-21, 27, 53-55, 57-58, 60-64, and 79-145 of co-pending U.S. Application No. 10/033,101 is respectfully requested.

CONCLUSION

It is respectfully submitted in view of the foregoing Remarks that all of the rejections in the Office Action dated January 15, 2003, have been overcome and should be withdrawn. Accordingly, reconsideration and withdrawal of the outstanding rejections and allowance of claims 211-394 is respectfully solicited, and the Office is respectfully requested to pass this application to issue. If, in the opinion of the Office, a telephone conference would expedite the prosecution of the subject application, the Office is invited to call the undersigned attorney at (312) 701-8775.

Respectfully submitted,

By: 

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Amendments to the Claims as of April 9, 2003

Claims 33, 35-36, 41-42, 45, 48-49, 57-59, 62, 64, 75-83, 88-93, 97-99 and 101-210 have been cancelled.

211. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject, wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction.

212. (New) The method of claim 211, wherein the pharmaceutical comprises at least one of: sildenafil citrate, pentoxifylline, yohimbine, apomorphine, alprostadil, papaverine, or phentolamine, or a combination, salt, or enantiomer thereof.

213. (New) The method of claim 211, wherein the pharmaceutical comprises at least one of a phosphodiesterase inhibitor or a dopamine receptor agonist, or a combination, salt, or enantiomer thereof.

214. (New) The method of claim 213, wherein the phosphodiesterase inhibitor is at least one of type III, type IV, or type V, and mixtures thereof.

215. (New) The method of claim 214, wherein the phosphodiesterase inhibitor is type V.

216. (New) The method of claim 211, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

217. (New) The method of claim 211, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

218. (New) The method of claim 211, wherein the composition comprises testosterone, alcohol, a penetration enhancer, and a gelling agent.

219. (New) The method of claim 218, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

220. (New) The method of claim 219, wherein the penetration enhancer is isopropyl myristate.

221. (New) The method of claim 218, wherein the gelling agent comprises polyacrylic acid.

222. (New) The method of claim 218, wherein the alcohol is selected from the group consisting of: ethanol and isopropyl.

223. (New) The method of claim 218, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

224. (New) The method of claim 223, wherein the composition further comprises sodium hydroxide.

225. (New) The method of claim 224, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl

monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

226. (New) The method of claim 211, wherein the composition and the pharmaceutical are components of a kit.

227. (New) The method of claim 211, wherein the subject is eugonadal or hypogonadal.

228. (New) The method of claim 211, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

229. (New) The method of claim 211, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

230. (New) The method of claim 211, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

231. (New) The method of claim 211, wherein the composition is administered at least once per day.

232. (New) The method of claim 231, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

233. (New) The method of claim 233, wherein the composition is administered to the subject for approximately 7 days.

234. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject, wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction, and

wherein the method is more effective in treating erectile dysfunction than a method comprising the administration of either the pharmaceutical or the composition alone.

235. (New) The method of claim 234, wherein the pharmaceutical comprises at least one of: sildenafil citrate, pentoxifylline, yohimbine, apomorphine, alprostadil, papaverine, or phentolamine, or a combination, salt, or enantiomer thereof.

236. (New) The method of claim 234, wherein the pharmaceutical comprises at least one of a phosphodiesterase inhibitor or a dopamine receptor agonist, or a combination, salt, or enantiomer thereof.

237. (New) The method of claim 236, wherein the phosphodiesterase inhibitor is at least one of type III, type IV, or type V, and mixtures thereof.

238. (New) The method of claim 237, wherein the phosphodiesterase inhibitor is type V.

239. (New) The method of claim 234, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

240. (New) The method of claim 234, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

241. (New) The method of claim 234, wherein the composition comprises testosterone, alcohol, a penetration enhancer, and a gelling agent.

242. (New) The method of claim 241, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

243. (New) The method of claim 242, wherein the penetration enhancer is isopropyl myristate.

244. (New) The method of claim 241, wherein the gelling agent comprises polyacrylic acid.

245. (New) The method of claim 241, wherein the alcohol is selected from the group consisting of: ethanol and isopropyl.

246. (New) The method of claim 241, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

247. (New) The method of claim 246, wherein the composition further comprises sodium hydroxide.

248. (New) The method of claim 247, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

249. (New) The method of claim 234, wherein the composition and the pharmaceutical are components of a kit.

250. (New) The method of claim 234, wherein the subject is eugonadal or hypogonadal.

251. (New) The method of claim 234, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

252. (New) The method of claim 234, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

253. (New) The method of claim 234, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

254. (New) The method of claim 234, wherein the composition is administered at least once per day.

255. (New) The method of claim 254, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

256. (New) The method of claim 255, wherein the composition is administered to the subject for approximately 7 days.

257. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject, wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction, and

wherein the method results in a synergistic effect.

258. (New) The method of claim 257, wherein the pharmaceutical comprises at least one of: sildenafil citrate, pentoxifylline, yohimbine, apomorphine, alprostadil, papaverine, or phentolamine, or a combination, salt, or enantiomer thereof.

259. (New) The method of claim 257, wherein the pharmaceutical comprises at least one of a phosphodiesterase inhibitor or a dopamine receptor agonist, or a combination, salt, or enantiomer thereof.

260. (New) The method of claim 259, wherein the phosphodiesterase inhibitor is at least one of type III, type IV, or type V, and mixtures thereof.

261. (New) The method of claim 260, wherein the phosphodiesterase inhibitor is type V.

262. (New) The method of claim 257, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

263. (New) The method of claim 257, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

264. (New) The method of claim 257, wherein the composition comprises testosterone, alcohol, a penetration enhancer, and a gelling agent.

265. (New) The method of claim 264, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

266. (New) The method of claim 265, wherein the penetration enhancer is isopropyl myristate.

267. (New) The method of claim 264, wherein the gelling agent comprises polyacrylic acid.

268. (New) The method of claim 264, wherein the alcohol is selected from the group consisting of: ethanol and isopropyl.

269. (New) The method of claim 264, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

270. (New) The method of claim 269, wherein the composition further comprises sodium hydroxide.

271. (New) The method of claim 270, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

272. (New) The method of claim 257, wherein the composition and the pharmaceutical are components of a kit.

273. (New) The method of claim 257, wherein the subject is eugonadal or hypogonadal.

274. (New) The method of claim 257, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

275. (New) The method of claim 257, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

276. (New) The method of claim 257, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

277. (New) The method of claim 257, wherein the composition is administered at least once per day.

278. (New) The method of claim 277, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

279. (New) The method of claim 278, wherein the composition is administered to the subject for approximately 7 days.

280. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject, wherein the pharmaceutical is selected from the group consisting of: phosphodiesterase inhibitors and dopamine receptor agonists,

wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction.

281. (New) The method of claim 280, wherein the pharmaceutical comprises sildenafil citrate or apomorphine or a combination, salt, or enantiomer thereof.

282. (New) The method of claim 280, wherein the phosphodiesterase inhibitor is at least one of type III, type IV, or type V, and mixtures thereof.

283. (New) The method of claim 282, wherein the phosphodiesterase inhibitor is type V.

284. (New) The method of claim 280, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

285. (New) The method of claim 280, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

286. (New) The method of claim 280, wherein the composition comprises testosterone, alcohol, a penetration enhancer, and a gelling agent.

287. (New) The method of claim 286, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

288. (New) The method of claim 287, wherein the penetration enhancer is isopropyl myristate.

289. (New) The method of claim 286, wherein the gelling agent comprises polyacrylic acid.

290. (New) The method of claim 286, wherein the alcohol is selected from the group consisting of: ethanol and isopropyl.

291. (New) The method of claim 286, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

292. (New) The method of claim 291, wherein the composition further comprises sodium hydroxide.

293. (New) The method of claim 292, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

294. (New) The method of claim 280, wherein the composition and the pharmaceutical are components of a kit.

295. (New) The method of claim 280, wherein the subject is eugonadal or hypogonadal.

296. (New) The method of claim 280, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

297. (New) The method of claim 280, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

298. (New) The method of claim 280, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

299. (New) The method of claim 280, wherein the composition is administered at least once per day.

300. (New) The method of claim 299, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

301. (New) The method of claim 300, wherein the composition is administered to the subject for approximately 7 days.

302. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject selected from the group consisting of: sildenafil citrate, pentoxifylline, yohimbine, apomorphine, alprostadil, papaverine, and phentolamine,

wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction.

303. (New) The method of claim 302, wherein the pharmaceutical comprises sildenafil citrate or apomorphine or a combination, salt, or enantiomer thereof.

304. (New) The method of claim 302, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

305. (New) The method of claim 302, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

306. (New) The method of claim 302, wherein the composition comprises testosterone, alcohol, a penetration enhancer, and a gelling agent.

307. (New) The method of claim 306, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

308. (New) The method of claim 307, wherein the penetration enhancer is isopropyl myristate.

309. (New) The method of claim 306, wherein the gelling agent comprises polyacrylic acid.

310. (New) The method of claim 306, wherein the alcohol is selected from the group consisting of: ethanol and isopropyl.

311. (New) The method of claim 306, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

312. (New) The method of claim 311, wherein the composition further comprises sodium hydroxide.

313. (New) The method of claim 312, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol,

propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

314. (New) The method of claim 302, wherein the composition and the pharmaceutical are components of a kit.

315. (New) The method of claim 302, wherein the subject is eugonadal or hypogonadal.

316. (New) The method of claim 302, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

317. (New) The method of claim 302, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

318. (New) The method of claim 302, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

319. (New) The method of claim 302, wherein the composition is administered at least once per day.

320. (New) The method of claim 319, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

321. (New) The method of claim 320, wherein the composition is administered to the subject for approximately 7 days.

322. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone, a gelling agent, and a penetration enhancer to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject selected from the group consisting of: sildenafil citrate, pentoxifylline, yohimbine, apomorphine, alprostadil, papaverine, and phentolamine,

wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction.

323. (New) The method of claim 322, wherein the pharmaceutical comprises sildenafil citrate or apomorphine or a combination, salt, or enantiomer thereof.

324. (New) The method of claim 322, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

325. (New) The method of claim 322, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

326. (New) The method of claim 322, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

327. (New) The method of claim 326, wherein the penetration enhancer is isopropyl myristate.

328. (New) The method of claim 322, wherein the gelling agent comprises polyacrylic acid.

329. (New) The method of claim 322, wherein the composition comprises alcohol selected from the group consisting of: ethanol and isopropyl.

330. (New) The method of claim 322, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

331. (New) The method of claim 330, wherein the composition further comprises sodium hydroxide.

332. (New) The method of claim 331, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

333. (New) The method of claim 322, wherein the composition and the pharmaceutical are components of a kit.

334. (New) The method of claim 322, wherein the subject is eugonadal or hypogonadal.

335. (New) The method of claim 322, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

336. (New) The method of claim 322, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

337. (New) The method of claim 322, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

338. (New) The method of claim 322, wherein the composition is administered at least once per day.

339. (New) The method of claim 338, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

340. (New) The method of claim 339, wherein the composition is administered to the subject for approximately 7 days.

341. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone, a gelling agent, and a penetration enhancer to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject,

wherein the pharmaceutical is sildenafil citrate or apomorphine, or a combination, salt, or enantiomer thereof; and

wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction.

342. (New) The method of claim 341, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

343. (New) The method of claim 341, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

344. (New) The method of claim 341, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

345. (New) The method of claim 344, wherein the penetration enhancer is isopropyl myristate.

346. (New) The method of claim 341, wherein the gelling agent comprises polyacrylic acid.

347. (New) The method of claim 341, wherein the composition further comprises alcohol selected from the group consisting of: ethanol and isopropyl.

348. (New) The method of claim 341, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

349. (New) The method of claim 348, wherein the composition further comprises sodium hydroxide.

350. (New) The method of claim 349, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

351. (New) The method of claim 341, wherein the composition and the pharmaceutical are components of a kit.

352. (New) The method of claim 341, wherein the subject is eugonadal or hypogonadal.

353. (New) The method of claim 341, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

354. (New) The method of claim 341, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

355. (New) The method of claim 341, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

356. (New) The method of claim 341, wherein the composition is administered at least once per day.

357. (New) The method of claim 356, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

358. (New) The method of claim 357, wherein the composition is administered to the subject for approximately 7 days.

359. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone, a gelling agent, and a penetration enhancer to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject, wherein the pharmaceutical is sildenafil citrate or apomorphine, or a combination, salt, or enantiomer thereof;

wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction, and
wherein the method is more effective in treating erectile dysfunction than a method comprising the administration of either the pharmaceutical or the composition alone.

360. (New) The method of claim 359, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

361. (New) The method of claim 359, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

362. (New) The method of claim 359, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

363. (New) The method of claim 362, wherein the penetration enhancer is isopropyl myristate.

364. (New) The method of claim 359, wherein the gelling agent comprises polyacrylic acid.

365. (New) The method of claim 359, wherein the composition further comprises alcohol selected from the group consisting of: ethanol and isopropyl.

366. (New) The method of claim 359, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

367. (New) The method of claim 366, wherein the composition further comprises sodium hydroxide.

368. (New) The method of claim 367, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol,

propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

369. (New) The method of claim 359, wherein the composition and the pharmaceutical are components of a kit.

370. (New) The method of claim 359, wherein the subject is eugonadal or hypogonadal.

371. (New) The method of claim 359, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

372. (New) The method of claim 359, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

373. (New) The method of claim 359, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

374. (New) The method of claim 359, wherein the composition is administered at least once per day.

375. (New) The method of claim 374, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

376. (New) The method of claim 375, wherein the composition is administered to the subject for approximately 7 days.

377. (New) A method for treating erectile dysfunction in a male subject, comprising administering in combination:

a) a topical gel or cream composition comprising testosterone, a gelling agent, and a penetration enhancer to a male subject and

b) a pharmaceutical useful for treating erectile dysfunction in the subject,

wherein the pharmaceutical is sildenafil citrate or apomorphine, or a combination, salt, or enantiomer thereof;
wherein the composition and pharmaceutical are administered in amounts sufficient to treat the erectile dysfunction, and
wherein the method results in a synergistic effect.

378. (New) The method of claim 377, wherein the pharmaceutical is administered about 20 minutes to about 60 minutes before sexual intercourse.

379. (New) The method of claim 377, wherein the composition comprises about 0.5% to about 10% w/w of testosterone.

380. (New) The method of claim 377, wherein the penetration enhancer is selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes.

381. (New) The method of claim 380, wherein the penetration enhancer is isopropyl myristate.

382. (New) The method of claim 377, wherein the gelling agent comprises polyacrylic acid.

383. (New) The method of claim 377, wherein the composition further comprises alcohol selected from the group consisting of: ethanol and isopropyl.

384. (New) The method of claim 377, wherein the composition comprises about 0.5% to about 10% testosterone; about 30% to about 98% alcohol; about 0.1% to about 5% penetration enhancer; and about 0.1% to about 5% gelling agent, wherein the percentages are weight to weight of the composition.

385. (New) The method of claim 384, wherein the composition further comprises sodium hydroxide.

386. (New) The method of claim 385, wherein the composition comprises:

a) about 0.5% to about 10% testosterone;

b) about 30% to about 98% alcohol selected from the group consisting of ethanol and isopropanol;

c) about 0.1% to about 5% penetration enhancer, selected from the group consisting of: isostearic acid, octanoic acid, oleic acid, oleyl alcohol, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy)ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, and terpenes;

d) about 1% to about 5% sodium hydroxide; and

e) about 0.1% to about 5% gelling agent;

wherein the percentages are weight to weight of the composition.

387. (New) The method of claim 377, wherein the composition and the pharmaceutical are components of a kit.

388. (New) The method of claim 377, wherein the subject is eugonadal or hypogonadal.

389. (New) The method of claim 377, wherein the subject is a man, and the composition is administered to an area of skin selected from the group consisting of: arm, shoulder, abdomen, back, and thigh.

390. (New) The method of claim 377, wherein the composition is administered to the subject in an amount suitable to deliver to the skin about 25 mg to about 100 mg of testosterone per day.

391. (New) The method of claim 377, wherein the composition administered to the subject achieves a maximum serum testosterone concentration at about 16 hours to about 22 hours after administration of the composition.

392. (New) The method of claim 377, wherein the composition is administered at least once per day.

393. (New) The method of claim 392, wherein the composition is administered to the subject for a sufficient number of days so as to achieve a steady-state serum testosterone concentration.

394. (New) The method of claim 393, wherein the composition is administered to the subject for approximately 7 days.